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


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Tuberculin in Dermatology.

By A. RAVOGLI, Cincinnati.

Tuberculin as a curative means for tubercular diseases has not been fully appreciated by the majority of physicians, and this is the reason why it has been employed chiefly as a means of diagnosis. Two causes have operated to prevent a general use of this valuable agent: One, a great expectation; the other, a fear of waking up the tubercle bacilli lying dormant in the system. The newspapers were singing "Glory, Halleluja that the remedy for the most dreaded disease had been discovered; physicians injected tuberculin at any stage of pulmonary tuberculosis and the patients died as before. The aprioristic argument, post hoc, ergo propter hoc, brought about the easy conclusion that the remedy did not cure the patient, ergo the remedy is no good. No particular attention had been called to the mixed infection which takes place in the affected tissues, and, indeed, the staphylococci and the streptococci are the cause of the breaking down of the tubercular nodules, and consequently of the pyogenic symptoms.

The presence of the mixed infection is the explanation for the cure of tuberculosis with iodoform, with eucrophen, and any other antiseptic which has a remedial action on the septic bacteria. The use of creosote, so much in vogue to-day, and its benefit in tuberculosis, is due only to its antiseptic properties, and not to any specific action on the tubercular tissues. It is the same benefit which is derived by the high altitude, where the secondary bacteria are much fewer, and therefore the tubercular tissues do not break down and the patient does relatively well.

The action of tuberculin is directed to the tubercular tissues, upon which it displays its wonderful action. It does not produce a reinstatement of the disorganized tissues, as would be necessary after the destruction caused by the breaking down of the tubercular nodules, and in this way it is of no benefit in cases where the ulcerations are deep and destructive. In recent

cases, however, where the tubercular nodules are in their integrity, it acts directly against the bacillus, causing a leucocytosis. The leucocytes dispose of the tubercular tissue probably by their phagocytic action. The studies of Goldman support this opinion.¹ He studied the synovial membrane of a tubercular knee-joint in a patient who had been treated with Koch tuberculin. The protoplasm of the giant cells were not equally stained, showing vacuoles and the nuclei were pale violet. All around the giant cell in the axis opposite the nucleus, a large number of leucocytes strongly stained were aggregated. This showed a regressive process of these protoplasm cells. The round cells, too, had suffered a partial necrosis.

I must limit myself to the action of tuberculin on tubercular affections of the skin. This organ offers a great advantage above all internal tissues, in that we can see the changes which take place and the results which are obtained. It is, therefore, the very organ which can give us an idea of the different processes and of the local action displayed by the remedy.

It is beyond any doubt that a large series of diseases of the skin, from a superficial erythema to a deep vegetating ulcer, are the result of tuberculosis. Cutaneous tuberculosis, like syphilis, shows great differences in its clinical features, which could scarcely be reapproached one to another unless for the unicity of the cause. Hallopeau² distinguished two classes of cutaneous tuberculosis, bacillary and non-bacillary eruptions. In the first, the tubercle bacillus is concealed in the tissue of the skin, producing the characteristic nodules, like in lupus vulgaris. The second class of cases result from the toxins proceeding from the biological exchanges of the bacilli existing latent in the system.

¹ Über Rückbildung Vorgänge an Tuberculösen Riesenzellen. Centralblatt für Path. II Bd. No. 22.

² Sur les Rapports de la Tuberculose avec les maladies de la peau autres que le Lupus Vulgaire. Paris 1896.

Joseph McFarland³ complains of the appearance of stubborn urticaria after the injection of any anti-tubercular serum, and Bayet and Schlangreieff referred to cases of erythema lasting from twenty to thirty days in individuals affected with acute pulmonary tuberculosis. With the exception of these erythema we find that the different tubercular affections of the skin are of bacillary nature. Some of them are the expression of general tuberculosis in the individual, like lichen scrofulosorum, diffused tubercular ulcerations, etc.; others are localized tuberculosis, limited to the affected place, i. e., lupus vulgaris. In some of these cases the ulcerative affection may be the result of tubercular inoculation of the skin, either from other affected tissues, or from outside infection, like in tuberculosis verrucosa cutis. You will easily understand that the tubercular eruptions of the skin are of such a proteiform appearance as to reproduce many affections, such as lichen scrophulosorum, folliculitis, lupus vulgaris, lupus erythematosus, lupoid ulcerations, erythema induratum, tubercular lymphangitis, gumma, ending in tubercular ulcers.

This multiplicity of forms is due to the complex structure of the skin, which consists of so many tissues and organs, and therefore, according to the tissues and organs affected, the eruption has a different form.

The question is to prove the presence of the bacillus in the skin in order to establish the nature of these cutaneous affections. The skin, as any other tissue of the human body, is not an appropriate ground for the tubercle bacillus. In inferior animals the development of the tubercle bacilli is much more rapid in comparison with that which occurs in the human. This gives us the opportunity of inoculating the suspected tissues on the guinea pigs, which is one of the best means to prove the tubercular nature.

In the cutaneous tubercular affections the finding of the tubercle bacillus is very difficult, and it requires a great deal of patience and time to be able to demonstrate its presence. The tubercle bacillus in the skin remains sometimes dormant for a long time without producing any infection. It remains only a potentiality, which after a long time is able to show its

presence. In cases of lupus vulgaris we see that after some years since the recovery, from the old scars it begins its work of local infection.

Tuberculin is a great agent for discovering the presence of the tubercle bacillus by the reaction produced in persons affected with tuberculosis. This statement I make from my experience and that of a large number of clinicians.

Since the first introduction of tuberculin to the present time it would be impossible to review the enormous literature on the subject, and while we find many authors very enthusiastic on the results, we find many others not only dissatisfied with its use, but ready to condemn this remedy. Hallopeau, Haslund and Prospelow speak against the use of tuberculin. Their experiments, they say, gave no results. Solomon Solis, under the title of Tuberculosis,⁴ has a dreadful report against tuberculin, and he refers to the words of Da Costa, accusing the physicians using tuberculin of cruelty and criminality.

At the congress of the German dermatologists in Leipsig, September, 1891, Kaposi spoke on the treatment of lupus with tuberculin. He admitted the remarkable reaction produced by this agent on the lupus nodules, and admitted, also, an improvement in the general and local condition. He denied, however, the diagnostic value of it, on account of its reaction in other affections, and he denied, also, the results as a curative means. Neisser took the stand against Kaposi, declaring tuberculin to be of great value, as being able through the reaction and the serous effusion in the affected tissues to remove the bacilli. He declared, furthermore, the tuberculin treatment as useful in opposing tubercular diathesis by the circulation in the system of an antitubercular remedy, able by its inflammatory action to cause the reabsorption of the tubercular infiltration.

At the same time H. Leslie Roberts⁵ of Liverpool referred to the action of tuberculin as a partial one. He admits, however, that under its influence the cells and serum infiltrating the tissues are re-

⁴ A System of Practical Therapeutics, edited by H. A. Hare, Philadelphia, Vol. III.

⁵ Klinische Beobachtungen über die Wirkung von Tuberculin auf Lupus. Monh für Pract. Derm., July, 1891.

³ Journal of the A. M. A. Aug. 1897.

moved and the skin takes on a more healthy appearance.

P. J. Eichhoff referred to the cases of lupus cured with tuberculin⁶ and to others much improved, and he advises in these cases to combine with the tuberculin treatment other local means to secure a permanent recovery.

H. Krause,⁷ Sonnenburg,⁸ Konrad Port,⁹ W. Van Hoorn,¹⁰ Sacchi¹¹ and many others have referred to cases of lupus successfully treated with tuberculin. The case referred to by Sacchi was lupus erythematosus, and he wrote that the recovery of this affection by tuberculin injection is a new proof of the tubercular nature of this disease, praising tuberculin as a great diagnostic means in discovering the tubercular nature of cutaneous affections.

Radcliffe Crocker¹² spoke very favorably of the use of tuberculin in lupus vulgaris. He very carefully described the symptoms, following the injection, upon the general system and on the affected locality. The local symptoms are like those which we have remarked in lupus erythematosus: redness of the affected areas, swelling and effusion of serum in the affected tissues.

Franklin W. White¹³ referred to 123 cases where tuberculin was used for diagnostic purposes. In fifty-seven cases tuberculin was injected, without reaction, as a test, and no evidence of tuberculosis was found in any of the non-reacting cases. From his observations he came to the conclusion that an absence of reaction after injection indicates almost invariably an absence of tuberculosis; the presence of reaction indicates the presence of tuberculosis more than four times out of five.

James T. Whittaker¹⁴ of Cincinnati, who since the first introduction of tuberculin by S. P. Kramer of this city has pursued his studies with patience and accuracy, recently read a paper before the Academy of Medicine of Cincinnati, "Six

years with Tuberculin," in which he gave a full account of his wide experience in the use of this remedy. He is not reticent in his judgment and frankly proclaims it to constitute the very best agent in diagnosis and the best single remedy we have for the treatment of this disease. What Whitaker says on tuberculin in tuberculosis of the lungs and internal organs, I am ready to apply to the tuberculosis of the skin.

The experience which I have had with this remedy and the encouraging results have convinced me of its efficacy both for diagnostic and for therapeutic purposes.

The only way to determine with certainty the tubercular nature of a disease is to find the tubercle bacillus in the tissues. You know, however, how difficult it is to find the germ in the skin, where sometimes it is necessary to make hundreds of sections before finding it. Another means is the inoculation of suspected detritus into the lower animals, which are more susceptible to tuberculosis. This is probably the best test, but it is not always at hand, while one injection with two milligrammes of tuberculin is always ready, and after a few hours the reaction can be easily seen.

I began to use tuberculin as a diagnostic means in two cases of ulcerative forms of the skin, where tuberculosis was suspected. One injection of two milligrammes of tuberculin produced general reaction, raising the temperature to 102° and 103° F. A local reaction on the ulcers was very remarkable, showing swelling and intense redness of the surrounding tissues. After the reaction had subsided, the condition of the ulcers was found greatly improved. This result encouraged me to continue the tuberculin injections, and in a few weeks the ulcers had entirely cicatrized. The ulcers dated back nearly three years and had been treated with antisiphilic remedies without result. In both cases the action of tuberculin showed it plainly to be not only a diagnostic aid, but also a therapeutic agent.

Lupus erythematosus is considered today without doubt as a tubercular affection. Hallopeau and Jeanselme have often found cases of lupus erythematosus accompanied with acute miliary tuberculosis. Besnier maintains that lupus erythematosus is a manifestation of an attenuated tu-

⁶ Therap. Monatsch. 1891. No. 9.

⁷ Deutsch. Med. Woch. 1891. No. 1.

⁸ Deutsch. Med. Woch. 1891. No. 28.

⁹ Munchener Med. Abhandlung 23, Heft. III.

¹⁰ Monhefte für Pract. Derm. 15 Dec., 1892.

¹¹ Riforma Medica. 1893. No. 169.

¹² A System of Pract. Therapeutics, edited by H. A. Hare, Philadelphia, Vol. III.

¹³ Boston Med. and Surgical Journal, Aug. 5, 1897.

¹⁴ Cincinnati Lancet and Clinic, Sept. 11, 1897.

berculosis much less than in lupus vulgaris. The inoculations of affected skin in the guinea pig did not give positive results, but Leloir succeeded by inoculating a piece of affected skin in the interior chamber of the eye of the rabbit. Sacchi¹⁵ referred to a case of recovery of lupus erythematosus with tuberculin. He remarked that this is a new proof of the tubercular nature of this disease, and a great diagnostic means to discover the tubercular nature of cutaneous affections.

I. A gentleman, F. T., aged 42, of good physique, has suffered for three years with lupus erythematosus diffusus of the whole face, and of the back and palm of both hands, and lupus ulcerations in the mucous membrane of the nose. The face, with very few healthy spots, was red, of a coppery hue, covered with greasy scales; the scales, firmly adherent, were deep in the ducts of the sebaceous glands. In some places, especially on the cheeks and the auriculæ, the eruption consisted of large, thick papules, depressed in the center, coalescent, forming a deep infiltration resembling lupus vulgaris. The hands were covered with the same eruptions, depressed in the center, and the whole palm of both hands and of the fingers were covered with the same eruption. The mucous membrane of the nose was infiltrated, bleeding easily, painful and reproduction of lupus were remarkable on the palate and tongue. The general condition was not very good, the patient was complaining of malaise, loss of appetite and slight fever at night. For three years he had been treated with every remedy externally and internally without any improvement. I found it to be a case for the use of tuberculin and injected in the scapular region two milligrammes of tuberculin (old). Nearly six hours later the patient was taken very ill with pain in his knees and back, nausea, and his temperature reached 104° F. The face and hands were swollen, red and cedematous.

I did not see the gentleman for one week. When he returned the local condition of the face was remarkably improved, the color nearly normal, no swelling, scarcely a sign of scaliness, with the exception of some infiltration in the auriculæ and on the nose. The condition of the mucous membrane of the nose was

much improved. Injections have been repeated from time to time, increasing the dose to five milligrammes. At present he looks nearly well; superficial scars are perceptible all over the face. The reaction is not so marked as it was in the beginning. There remains only a little infiltration around both ears. Locally I used a salve containing resorcin, salicylic acid and creosote, which completed the cure of the affected surface. The gentleman is exceedingly gratified. He considers himself thoroughly well.

II. Another no less interesting case I had in a lady 38 years old, a Sister of Charity. She is of a good physique, and has enjoyed the best of health. Father and mother are still living, healthy; six sisters are also in good health. Although her regular occupation has been that of teaching school, she has often attended patients. Over two years ago she noticed a small red spot on her left cheek, which gradually extended, and later another appeared on the right side, covering gradually the cheeks and the nose in a red, coppery hue, giving the appearance of a butterfly. Gradually the disease spread to the orbital regions, then affected the forehead, the neck and spread on the scalp. Lately the affection spread onto the body, arms, hands, feet, shoulders, and attacked the scalp, causing total alopecia. The spots consisted of red elevations of the skin, depressed in the center and coalescing. The lips, tongue and palate were also covered with red spots. The eruption lately had spread to the hands, fingers, arms and feet. A bloody exudation had taken place on the nose, cheek and eyelids, giving a black appearance to the surface.

Her general health had run down considerably; no appetite; loss of sleep; fever toward evening; malaise, and great discouragement.

All remedies had been employed with no result. Three months ago I gave to her the first injection of tuberculin (old), one milligramme. The reaction was somewhat intense, temperature raised to 101° F., with some swelling and cedema of the face. Two days later she received another of three milligrammes. The reaction was very much more marked, raising the temperature to 105°, with nausea, vomiting and pains in the limbs. After three days the temperature went down to normal and the affected skin began to show

¹⁵ *Riforma Medica*. 1893. No. 169.

a marked improvement. The bloody effusion in the face began to disappear, the eruption began to diminish and the swelling to subside. Her general condition under the tuberculin treatment began to improve. I was encouraged from the result of the first case, and from her improvement, and determined to continue the use of tuberculin. We began the injections with the new tuberculin T. R., one injection every other night, increasing the dose to 5-500 milligramme. The reaction obtained was nearly imperceptible, and the local condition, although somewhat improved, yet after twelve injections remained unchanged. From the new tuberculin we returned to the old, never exceeding the dose of three milligrammes for each injection.

The reaction is always remarkable, temperature raising to 101° and 102° F.; with redness and swelling of the affected skin, which after the reaction subsides appears nearly well. After two months' treatment the face is nearly well. There remain a few points of infiltration, which I treat locally by means of electrolysis. The scalp is nearly well; alopecia is now complete. The arms and the hands have recovered; once in a while a new, little papule comes on her fingers. The skin where the eruption was shows a great number of superficial scars, which are nothing more than atrophic points, resulting from the reabsorption of the infiltration from the affection. The mucous membrane of the lips, mouth, tongue, palate, nose and eyes is much improved, and the patient feels much better in her general health and is very much quicker in mind. While using tuberculin injections we do not neglect the local treatment. Salves of Resorcin, salicylic acid and creosote are applied on the skin twice a day. I must say that so far the treatment has been encouraging. The local treatment which, without the tuberculin injections, had given no results, now in association with this constitutional agent has been of great value.

III. Miss M. T., a fourteen-year-old girl, has been affected with ichthyosis hystrix since infancy. Her parents are living, but they do not enjoy the best of health, suffering at times with bronchial affections. Both, however, never had any skin trouble. An eruption had spread all over her body in the form of small red elevations of the

skin, coalescent and covered with thick, adherent scales. The eruption, in the form of small, thick warts, was general on the body, face, scalp and limbs, and the back and palm of the hands and back and soles of the feet. The disposition of the eruption in some places followed exactly the ramifications of the nerves beneath, especially on the arms and legs. She had never perspired; at times the eruption was so thick that it prevented her from moving. She received every treatment recommended in this disease. Every kind of medicated baths, inunctions with cod liver oil, tar, and different salves, in one word, every remedy recommended was faithfully applied, with little or no result. The parents sent the girl under my care to a private hospital. From my previous experience I was somewhat discouraged. She was suffering at that time with ulcerations of the cornea of the right eye, and also an otitis media purulenta.

Although ichthyosis is considered a form of keratosis, which has nothing to do with any tubercular affection, yet I thought that ichthyosis could exist in a tubercular subject. On June 27th of this year I gave her an injection of new tuberculin T. R., beginning with 1-500 mg. Her temperature rose to 101° F., with pain in her joints and lumbar region, headache, and locally the whole body where the eruption was, appeared intensely red. The injections were continued every other day, increasing each injection 1 cc., stopping at 5 cc.

In a few days the girl, who had never perspired in her life, became moist with a heavy perspiration. The eruption was covered with an unusual quantity of thick scales, which, falling off, left a smooth reddish surface. The condition of the patient, although a great deal better, yet she did not continue to improve as in the beginning, and the reaction after the injection became scarcely perceptible.

From the experience with the old tuberculin I began to inject 2 mg. of it. The reaction following the injection was much more marked, for the temperature arose to 103° F. Since then I kept on with the old tuberculin at the dose of 2 mg. for each injection. The patient at present takes only one injection per week. The ichthyosis condition is: The scalp thoroughly well; in the face there remains some little pigmentation, where the eruption lasted for so many years. The neck, chest

and shoulders show the skin smooth and clear. On the arms there remains a reddish discoloration, where the eruption was located, corresponding to the ramifications of the nerves. The arms are in the same condition; the hands on the tenar region and on the second finger show the skin somewhat dry and rough. The legs are still somewhat red and slightly scaly, but are improving considerably. The condition of the feet resembles somewhat that of the hands.

I am continuing the use of tuberculin, and I can say that the result, so far obtained, although not yet complete, is quite remarkable and encouraging.

The influence of tuberculin on this eruption shows that ichthyosis is a true disease of the skin, a chronic dermatitis, and not a simple anomaly of the epidermis. Likewise, it shows that the disease is the result of an autotoxic condition of the system, according to the opinion expressed by Tommasoli.¹⁶

M. Jadasohn has already established a relation between tuberculosis and pityriasis rubra (Hebra), and in my case we can see a relation between ichthyosis and the tubercular condition. It is possible that these dermatoses find a better ground for their development in individuals who have a tubercular diathesis.

In the limits of a small clinical report, I do not find myself prepared to enter into this discussion, which would consume a long time. I wish only to call your attention to the result obtained by tuberculin in an incurable disease. I wish to request you to try this agent in any case of this affection which you encounter in your practice.

In conclusion, I must say that I have used tuberculin with satisfactory results in several cases of ulcerative tuberculosis of the skin. As reported in this paper, I used tuberculin in two cases of L. E. disseminatus, which were greatly improved. You know the prognosis of L. E. disseminatus is usually fatal, tuberculosis, miliaris acuta, or pleuro-pneumonia being the end of the patients. Now, if in a disease with an ordinary fatal termination it has caused the disappearance of the disfiguring eruption, the removal of the night fever, the improvement of the digestive faculties, I should, and am, greatly indebted to the remedy and to its discoverer.

Similarly, ichthyosis hystrix is an incur-

able disease of the skin. We do not know its nature nor its cause. By the employment of tuberculin I have brought the disease nearly to a recovery. I do not argue whether tuberculin has acted upon the tubercular diathesis, probably latent in this little patient, or if it has counteracted the toxins existing in her system. It is possible that the leucocytosis induced by tuberculin in the already chronically infiltrated tissues of the derma, has caused the reabsorption of these infiltrating elements and the wonderful improvement of the affection.

From my experience I must say that, 1st, tuberculin is a great help in dermatology, both as a diagnostic and therapeutic means. I find that the assertion of several authors, that tuberculin causes reaction in many affections of the skin other than those of a tubercular nature is not exact. Lately I had a case of an eruption of both palms of the hand and fingers, which resembled greatly lupus erythematosus. I gave the patient one tuberculin injection of 2 mg. in the evening, requesting him to come back the following morning. He came back 12 hours after, had slept well, no pain or malaise had troubled him. The temperature was normal. The affection proved to be nothing else than an eczema, which in a few weeks was entirely well with the ordinary treatment.

2d. That in lupus erythematosus it acts remarkably well as a systemic treatment, but of course in the locality some external applications, like salves, cauterizations, electrolysis, etc., have to be applied so as to help to reduce the infiltrated places.

3d. That in a large quantity of injections I never had any bad effects, and the condemning of tuberculin for the fear of spreading tuberculosis is absolutely absurd.

4th. That the old tuberculin has given me more marked reaction, both general and local, than the new tuberculin, and so far I find in dermatological work the old preferable to the new.

5th. That in cases where no other remedy has any influence, and tuberculin causes the disappearance of the eruption, the healing of the ulcers, the improvement of the general condition, we have to acknowledge that it is a great remedy.

6th. That if relapses occur after ceasing the use of tuberculin, the remedy must not be blamed. It must be used for a long time, in small doses, at long intervals, until recovery is assured.

¹⁶Anñ. de Derm. and Syphil., 1893.

